INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WO 38705	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/06528	International filing date *(day/month/year)* 20.06.2003	Priority date *(day/month/year)* 21.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/20		
Applicant LEK PHARMACEUTICALS D.D. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.01.2004	28.09.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Estañol Y Cornella, Telephone No. +49 89 2399-8647

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/06528

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-13 as originally filed

Claims, Numbers

1-15 received on 31.08.2004 with letter of 31.08.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 11

   because:

   ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1,12-15
	No:	Claims	

2. Citations and explanations

   see separate sheet

Item III.
Claim 11 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Item V.
Reference is made to the following documents:

D1: WO 00 66089 A (CIMA LABS INC) 9 November 2000 (2000-11-09)
D2: US-B1-6 391 335 (KHANKARI RAJENDRA K ET AL) 21 May 2002 (2002-05-21)
D3: US-B1-6 368 625 (KHANKARI RAJENDRA K ET AL) 9 April 2002 (2002-04-09)
D4: US-B1-6 200 604 (KHANKARI RAJENDRA K ET AL) 13 March 2001 (2001-03-13)
D5: US-A-6 117 451 (KUMAR VIJAI) 12 September 2000 (2000-09-12)
D6: US-A-5 985 823 (GOLDSTEIN BETH P) 16 November 1999 (1999-11-16)

D1 or D2 or D3 or D4 discloses orodispersible drug delivery systems comprising silicified microcrystalline cellulose (examples 1, 2 of D1, examples 1, 2 of D2, example 2 of D3 and example 1 of D4.
D5 or D6 discloses a rapid disintegrating tablet comprising (I) silicified microcrystalline cellulose and (ii) an hypoglycemic agent in D5 or an antibiotic in D6.

None of the cited documents discloses a rapidly disintegrating tablet comprising silicified microcrystalline cellulose and a mixture of clavulanic acid and amoxicillin. Thus, the subject-matter of present claims 1 and 11-15 is new over D1 or D2 or D3 or D4 or D5 or D6.

The subject-matter of claims 1, 11-15 does not meet the requirements of the PCT in respect of inventive step, the reasons being as follows:

The advantages of using silicified microcrystalline cellulose as the sole disintegrant in rapidly disintegrating tablets, including orodispersible tablets are known from the cited prior art. The selection of the combination of clavulanic acid and amoxicillin as active agent, as claimed in present claims 1, 11-15, can only be regarded as inventive, if it presents unexpected effects or properties in relation to the pharmaceutical formulations disclosed in the cited prior art. No such effects or properties are however indicated in

the application. Moreover, attention is drawn to the fact that Examples 1 or 2 of D1 or D2 disclose the proportion of the active agent, the proportion of the silicified microcrystalline cellulose and the ratio of the active substance and silicified microcrystalline cellulose which fall within the ranges disclosed in present claims 8-9.

Furthermore, the addition of hydrogenated castor oil as a lubricant is considered as one of the options which the skilled man would select without involving an inventive step.

For the assessment of the present claim 11 on the question whether it is industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims.